UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,851	04/18/2005	Patrice Tremble	PA1312	3970

28390 7590 01/22/2007

MEDTRONIC VASCULAR, INC.
IP LEGAL DEPARTMENT
3576 UNOCAL PLACE
SANTA ROSA, CA 95403

EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,851	TREMBLE ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *20-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4-18-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of group I, claims 1-19, in the reply filed on 12-21-06 is acknowledged.

2. Claims 20-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12-21-06.

Applicant's amendment filed 12-21-06 has been entered. Claims 1-28 are pending. Claims 1-19 are under consideration.

Specification

3. The disclosure is objected to because of the following informalities: The term "CLAIMS" on page 22 of the specification is improper. Changing the term "CLAIMS" to "We claim:" or "What is claimed is:" would be remedial.

Appropriate correction is required.

This application contains sequence disclosures that are encompassed by the definition for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821 (a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. There is no "sequence listing" submitted in the instant application. Applicant is required to submit a computer readable form (CRF) copy of the "sequence listing", a paper copy of the "sequence listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and, where

applicable, include no new mater as required by 37 CFR. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). It should be noted that response to the instant Official action would not be considered complete unless applicant complies with the requirements set forth above.

Furthermore, there is no sequence identifier for the nucleotide sequence in Figures 3A and 3B or in the "BRIEF DESCRIPTION OF THE DRAWINGS". Each nucleotide sequence is required to have a sequence identifier. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-19 are directed to a method of treating a vulnerable plaque associated with a blood vessel of a patient comprising providing at least one gene therapy agent, such as DNA or RNA, encoding at least one protein, administering said agent to a target cell population, expressing the protein, such as secreting the protein into a bloodstream or localized expression, from a portion of target cell population, and modifying the vulnerable plaque. Claim 3 specifies the gene therapy agent comprises a vector, such as a plasmid, retroviral vectors, adenoviral vectors, and Herpes Simplex vectors etc. Claim 4 specifies the administration comprises at least

one technique selected from the group consisting of injection, direct uptake, receptor-mediated uptake, IV, ingestion, electroporation, and precipitation. Claims 5-8 specify the in vivo gene therapy is administered with a balloon catheter device or stenting the blood vessel adjacent the vulnerable plaque, or insterstitially. Claims 9-11 specify the gene therapy agent is administered ex vivo. Claims 12-14 specify the protein is a collagen isoform, an A1 apolupoprotein isoform, or a mutant Milano isoform. Claim 15 specifies the target cell population comprises muscle cells, vascular cells, hepatic cells, harvested patient cells, and donor cells. Claim 19 specifies the modifying the vulnerable plaque comprises modification selected from fibrous cap reinforcement, reduction of lipid pool size, and modifying a lipid pool constitution etc., as recited in the claim.

The specification discuss a prophetic gene therapy method of treating a vulnerable plaque associated with a blood vessel of a patient by administering a gene therapy agent encoding at least one protein to a target cell population via in vivo or ex vivo administration (e.g. p. 5, 12-18).

The claims read on administering any naked DNA or RNA or a vector comprising a transgene encoding at least one protein to a target cell population of a patient for treating a vulnerable plaque associated with a blood vessel via various in vivo or ex vivo administration routes. The claims encompass using any DNA or RNA encoding any protein, such as collagen isoform, A1 apolipoprotein isoform, or mutant Milano isoform, for treating any vulnerable plaque associated with a blood vessel in a patient. Even each of the collagen isoform, the A1 apolipoprotein isoform, and mutant Milano isoform encompasses a genus of structural variants of corresponding wild type protein. The specification fails to provide adequate guidance and

evidence for how to treat any vulnerable plaque associated with a blood vessel in a patient with a DNA or RNA encoding at least one protein that could be any protein so as to provide therapeutic effect in vivo or ex vivo.

It was known in the art that the amino acid sequence of a protein determines its structural and functional properties, and predictability of which amino acids can be removed from a protein's sequence and still result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Rudinger, 1976 (Peptide Hormones, Edited by Parsons, University Park Press, Baltimore, p. 1-7), points out that "The significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study" (e.g. p. 6). Kaye et al., 1990 (Proc. Natl. Acad. Sci. USA, Vol. 87, pp. 6922-6926) teaches that "A single amino acid substitution results in a retinoblastoma protein defective in phosphorylation and oncoprotein binding" (e.g. Title).

Skolnick et al., 2000 (Trends in Biotech, Vol. 18, p. 34-39) states "Sequence-based methods for function prediction are inadequate because of the multifunctional nature of proteins. However, just knowing the structure of the protein is also insufficient for prediction of multiple functional sites. Structural descriptors for protein functional sites are crucial for unlocking the secrets in both the sequence and structural-genomics projects" (e.g. abstract). Skolnick further states that "Knowing a protein's structure does not necessarily tell you its function" and "Because proteins can have similar folds but different functions, determining the structure of a protein may or may not tell you something about its function" (e.g. p. 36, box 2). In view of

such, each protein has its own particular biological function and different proteins have different biological functions. The biological function of a protein was unpredictable from mere amino acid sequence at the time of the invention. There is no evidence of record that any DNA or RNA encoding at least one protein would be able to treat any vulnerable plaque associated with a blood vessel in vivo or ex vivo. Thus, one skilled in the art at the time of the invention would not know how to use the claimed gene therapy agent encoding at least one protein to treat a vulnerable plaque associated with a blood vessel in vivo or ex vivo.

Further, the specification fails to provide a correlation between the gene therapy agent encoding at least one protein and the vulnerable plaque associated with a blood vessel. Absent specific guidance that a protein is correlated to the vulnerable plaque associated with a blood vessel in a patient, one skilled in the art at the time of the invention would not know how to use said gene therapy agent to treat a vulnerable plaque associated with a blood vessel in a patient.

In addition, the claims encompass using only a naked DNA or RNA encoding at least one protein without a vector comprising a promoter and other element necessary for the expression of said at least one protein. It was well known in the art that a protein has to be expressed in order to elicit its biological function. A DNA or RNA lacking the elements required for its expression would not express the encoded protein, therefore, said DNA or RNA would not be able to provide therapeutic effect for treating a vulnerable plaque associated with a blood vessel in vivo or ex vivo. Thus, one skilled in the art at the time of the invention would not know how to use those DNA or RNA to treat any vulnerable plaque associated with a blood vessel in vivo or ex vivo.

In view of the reasons set forth above, one skilled in the art at the time of the invention would require determination and characterization of the biological function of the protein encoded by the gene therapy agent as claimed, determination of the correlation between the protein encoded by said gene therapy agent and the vulnerable plaque associated with a blood vessel, trial and error experimentation to determine how to use said gene therapy agent to treat said vulnerable plaque, and trial and error experimentation to determine whether said gene therapy agent would be able to provide therapeutic effect for treating said vulnerable plaque.

The specification also fails to provide adequate guidance and evidence for how to administer at least one gene therapy agent encoding at least one protein to treat any vulnerable plaque associated with a blood vessel in a patient via various administration routes in vivo or ex vivo such that therapeutic effect can be obtained for treating said vulnerable plaque. The claims encompass using any naked DNA or RNA, any vector expressing at least one protein to treat a vulnerable plaque associated with a blood vessel via various administration routes, including oral administration, intravenous administration, intraperitoneal administration, direct injection, infusion, intramuscular injection, subcutaneous administration, and intramedullary administration etc. The claims read on gene therapy in vivo or ex vivo.

The nature of the invention being gene therapy, the state of the prior art was not well developed and is highly unpredictable. Eck et al., 1996 (Goodman & Gilman's The Pharmacological Basis of Therapeutics, McGraw-Hill, New York, p. 77-101) reports that numerous factors complicate in vivo gene therapy with respect to predictably achieving levels and duration of gene expression which have not been shown to be overcome by routine experimentation. These include, the fate of the DNA vector itself (volume of distribution, rate of

clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. These factors differ dramatically based on the vector used, the protein being produced, and the disease being treated (e,g, bridging pages 81-82). The specification fails to provide adequate guidance for how to overcome any of the above unpredictable parameters in the gene therapy art such that one would be able to obtain sufficient expressed protein to provide therapeutic effect in target cell population in a patient. It is important to note that treatment encompass complete amelioration of symptoms associated with the vulnerable plaque associated with a blood vessel. The specification fails to provide adequate guidance for how the administration of at least one gene therapy agent encoding at least one protein to a target cell population via various administration routes would be able to provide therapeutic effect for treating said vulnerable plaque.

Further, vector targeting to desired tissues in vivo continues to be unpredictable and inefficient as supported by numerous teachings in the art. For example, Deonarain (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicates that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art which show promise but states that such techniques are even less efficient than viral gene delivery (see page 65, first

paragraph under Conclusion section). Verma (Sept. 1997, Nature, Vol. 389, pages 239-242) reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (see entire article). Verma states that "The Achilles heel of gene therapy is gene delivery, and this is the aspect that we will concentrate on here. Thus far, the problem has been an inability to deliver genes efficiently and to obtain sustained expression...The use of viruses (viral vectors) is powerful technique, because many of them have evolved a specific machinery to deliver DNA to cells, However, humans have an immune system to fight off the virus, and our attempts to deliver genes in viral vectors have been confronted by these host responses." (e.g. p. 239, column 3). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Crystal (1995, Science, Vol. 270, page 404-410) also reviews various vectors known in the art and points out that "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409).

In addition, Gorecki, 2001 (Expert Opin. Emerging Drugs, 6(2): 187-198) reports that "the choice of vectors and delivery routes depends on the nature of the target cells and the required levels and stability of expression" for gene therapy, and obstacles to gene therapy *in vivo* include "the development of effective clinical products" and "the low levels and stability of expression and immune responses to vectors and/or gene products" (e.g. abstract). Nabel (Circulation, 1995, pp. 1-17) teaches that myocardial gene therapy has been hindered by limited transfection efficiency, transient expression of recombinant genes, and vectors that have

provoked inflammatory responses (e.g. p. 5-6, Myocyte Gene Transfer). It appears that several factors, including the DNA sequence used, the type of vector used, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, the biological function of the protein, and the administration route, play important role in determining the efficiency of gene transfer and gene therapy in vivo and ex vivo. Those factors contribute to the unpredictability of gene therapy in vivo or ex vivo, which could not be overcome by routine experimentation.

In view of the unpredictability of in vivo gene therapy in general, the broad scope of the gene therapy agent used, the unpredictability of the protein function from mere amino acid sequence, and the lack of correlation between the biological function of the protein and the vulnerable plaque associated with a blood vessel, one skilled in the art at the time of the invention would not know how to treat the vulnerable plaque associated with a blood vessel by administering at least one gene therapy agent encoding at least one protein via various administration routes such that expression of said protein would be able to provide therapeutic effect for treating said vulnerable plaque in vivo or ex vivo.

For the reasons discussed above, it would have required undue experimentation for one skilled in the art at the time of the invention to practice over the full scope of the invention claimed. This is particularly true given the nature of the invention, the state of the prior art, the breadth of the claims, the level of one of ordinary skill which is high, the amount of experimentation necessary, the lack of working example and scarcity of guidance in the specification, and the unpredictable nature of the art.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1, 2, 4-7, 9, 15-17 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Mandrusov et al., 2006 (US Patent No. 7,008,411 B1).

Claims 1, 2, 4-7, 9, 15-17 and 19 are directed to a method of treating a vulnerable plaque associated with a blood vessel of a patient comprising providing at least one gene therapy agent, such as DNA or RNA, encoding at least one protein, administering said agent to a target cell population, expressing the protein, such as secreting the protein into a bloodstream or localized expression, from a portion of target cell population, and modifying the vulnerable plaque. Claim 4 specifies the administration comprises at least one technique selected from the group consisting of injection, direct uptake, receptor-mediated uptake, IV, ingestion, electroporation, and precipitation. Claims 5-7 specify the in vivo gene therapy is administered with a balloon catheter device or stenting the blood vessel adjacent the vulnerable plaque. Claim 9 specifies the gene therapy agent is administered ex vivo. Claim 15 specifies the target cell population comprises muscle cells, vascular cells, hepatic cells, harvested patient cells, and donor cells. Claim 19 specifies the modifying the vulnerable plaque comprises modification selected from fibrous cap

reinforcement, reduction of lipid pool size, and modifying a lipid pool constitution etc., as recited in the claim.

Mandrusov teaches a method of treating coronary artery and related disease including vulnerable plaque with a therapeutic or biologically active agent (e.g. column 3, lines 42-59) through the bloodstream or vessel wall (e.g. column 5, lines 12-14) by using stent having the vulnerable plaque treating drug or agent dispersed on the surface of the stent (e.g. column 4, lines 41-43). Representative therapeutic or biologically active agents include VEGF, TGF-alpha, TGF-beta, IGF and G-CSF etc, genes encoding these proteins, and cells transfected with these genes (e.g. column 4, line 62 to column 5, line 11). Mandrusov also teaches a method for stabilizing a vulnerable plaque in a lumen wall by advancing a needle catheter near said vulnerable plaque and delivering a vulnerable plaque stabilizing agent with said needle catheter to fibrous cap without penetrating lipid core, and said stabilizing agent strengthens said fibrous cap or thickens said fibrous cap (e.g. column 20). A vulnerable plaque treating drug or biologically active agent may be injected through or around the fibrous cap of a vulnerable plaque with a needle catheter, and a drug eluting stent may be used to strength or increase the thickness of the fibrous cap of the vulnerable plaque in a controlled manner (e.g. column 5, lines 45-67). Cells transfected with genes indicates ex vivo treatment. Thus, claims 1, 2, 4-7, 9, 15-17 and 19 are anticipated by Mandrusov.

8. Claims 1-7, 9 and 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Hung et al., 1997 (WO 97/16169, IDS).

Claims 1-7, 9 and 15-18 are directed to a method of treating a vulnerable plaque associated with a blood vessel of a patient comprising providing at least one gene therapy agent, such as DNA or RNA, encoding at least one protein, administering said agent to a target cell population, expressing the protein, such as secreting the protein into a bloodstream or localized expression, from a portion of target cell population, and modifying the vulnerable plaque. Claim 3 specifies the gene therapy agent comprises a vector, such as a plasmid, retroviral vectors, adenoviral vectors, and Herpes Simplex vectors etc. Claim 4 specifies the administration comprises at least one technique selected from the group consisting of injection, direct uptake, receptor-mediated uptake, IV, ingestion, electroporation, and precipitation. Claims 5-7 specify the in vivo gene therapy is administered with a balloon catheter device or stenting the blood vessel adjacent the vulnerable plaque. Claim 9 specifies the gene therapy agent is administered ex vivo. Claim 15 specifies the target cell population comprises muscle cells, vascular cells, hepatic cells, harvested patient cells, and donor cells. Claim 18 specifies modulating expression level of the protein with an expression cassette.

Hung teaches a method of treating a cardiovascular indication in a patient by administering intrapericardially to a patient a pharmaceutical composition comprising a polynucleotide encoding TGF-alpha, TGF-beta, PGF, TNF-alpha VEGF, or tPA etc. (e.g. p. 58, claims 1, p. 64, claim 46). Cells can be removed from the pericardial space, transfected with a polynucleotide, and replaced to the pericardial space for expression of the polynucleotide (e.g. abstract). The polynucleotide comprises a viral vector, such as a retrovirus, an adenovirus, an adeno-associated virus, a herpes virus, a semliki forest virus, and a sindbis virus (e.g. claims 7 and 8). The cardiovascular indication is associated with coronary artery occlusion, including

lipid/cholesterol deposition and plaque rupture, and coronary artery restenosis (e.g. claims 15-17). The pericardial administration comprises injection, catheterization and cannulization etc. (e.g. claim 47). Cells removed from the pericardial space for transfection with a polynucleotide, and replaced back to the pericardial space constitutes ex vivo gene therapy. Thus, claims 1-7, 9 and 15-18 are anticipated by Hung.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system

provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER